Intraoperative fabrication of patient-specific moulded implants for skull reconstruction: single-centre experience of 28 cases

Stieglitz, Lennart Henning ; Gerber, Nicolas ; Schmid, Thomas ; Mordasini, Pasquale ; Fichtner, Jens ; Fung, Christian ; Murek, Michael ; Weber, Stefan ; Raabe, Andreas ; Beck, Jürgen

Abstract: BACKGROUND Intraoperatively fabricated polymethylmethacrylate (PMMA) implants based on computer-designed moulds were used to improve cosmetic results after hard tissue replacement. To assess the implant's cosmetic and functional results we performed both subjective and objective assessments. METHODS This retrospective analysis was performed using a cohort of 28 patients who received PMMA implants between February 2009 and March 2012. The cosmetic and functional results were assessed using a patient questionnaire. Furthermore an objective volumetric subtraction score (0-100) was applied and implant thickness, as well as gaps and tiers, were measured. RESULTS Patients mainly judged their cosmetic result as "good". Two of the 28 patients found their cosmetic result unfavourable. The functional result and stability was mainly judged to be good. Measurements of implant thickness showed a very high correlation with the thickness of the contralateral bone. Volumetric subtraction led to a median quality of 80 on a scale from 0 to 100. Median gaps around the margins of the implant were 1.5 mm parietally, 1.7 mm frontally and 3.5 mm fronto-orbitally, and median tiers were 1.2 mm, 0 mm and 0 mm respectively. The overall rate of surgical revisions was 10.7 % (three patients). Two patients suffered from wound healing disturbances (7.1 %). The overall complication rate was comparable to other reports in the literature. CONCLUSIONS Implantation of intraoperatively fabricated patient-specific moulded implants is a cost-effective and safe technique leading to good clinical results with a low complication rate.

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Intraoperative Fabrication of Patient-Specific Molded Implants for Skull Reconstruction: Single-Center Experience of 28 Cases

Lennart Henning Stieglitz, MD[1], Nicolas Gerber, PhD[2], Thomas Schmid[3], Pasquale Mordasini, MD[4], Jens Fichtner, MD[1], Christian Fung, MD[1], Michael Murek, MD[1], Stefan Weber, PhD[2], Andreas Raabe, MD[1], Jürgen Beck, MD[1]

[1] Department of Neurosurgery, Bern University Hospital, Bern, Switzerland
[2] ARTORG - ISTB, University of Bern, Bern, Switzerland
[3] University of Bern, Bern, Switzerland
[4] Diagnostic and Interventional Neuroradiology, Bern University Hospital, Bern, Switzerland

Corresponding Author:
Lennart Henning Stieglitz, MD
Department of Neurosurgery
Bern University Hospital
Freiburgstrasse 10
3010 Bern, Switzerland
e-mail: lennart@stieglitze.de
Tel: +41 31 632 2111
Fax: +41 31 632 0432

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Abstract

Background:

Intraoperatively fabricated polymethylmethacrylate (PMMA) implants based on computer-designed molds were used to improve cosmetic results after hard tissue replacement. To assess the implant's cosmetic and functional results we performed both subjective and objective assessments.

Methods:

This retrospective analysis was performed using a cohort of 28 patients who received PMMA implants between February 2009 and March 2012. The cosmetic and functional results were assessed using a patient questionnaire. Furthermore an objective volumetric subtraction score (0-100) was applied and implant thickness, as well as gaps and tiers, were measured.

Results:

Patients mainly judged their cosmetic result as "good". Two of the 28 patients found their cosmetic result unfavorable. The functional result and stability was mainly judged to be good. Measurements of implant thickness showed a very high correlation with the thickness of the contralateral bone. Volumetric subtraction led to a median quality of 80 on a scale from 0 to 100. Median gaps around the margins of the implant were 1.5 mm parietally, 1.7 mm frontally and 3.5 mm fronto-orbitally, and median tiers were 1.2 mm, 0 mm and 0 mm respectively. The overall rate of surgical revisions was 10.7% (3 patients). Two patients suffered from wound healing disturbances (7.1%). The overall complication rate was comparable to other reports in the literature.

Conclusions:

Implantation of intraoperatively fabricated patient-specific molded implants is a cost-effective and safe technique leading to good clinical results with a low complication rate.

Key words: hemicraniectomy, PMMA, PSI, PSMI, skull reconstruction

Introduction

Advances in neurosurgery and intensive care over the last two decades achieved great improvement in the outcomes of patients with severe head trauma, stroke, brain tumors and infectious diseases affecting the skull. Surgical treatment often involves a large osteoclastic craniotomy or delayed reimplantation of the autologous bone flap. In many of these cases a reconstruction of the skull is necessary because of 1) destruction of the bone as result of trauma, 2) infection, 3) tumor infiltration, or 4) aseptic necrosis and resorption of the bone flap [19].

There are several techniques and materials available for preservation of the explanted bone-flap and its replacement [2,5,7,12,13,16-18]. These techniques differ in functionality, cosmetic result, costs and spectrum of complications involved in the procedures. Among the artificial materials, polymethylmethacrylate (PMMA) is the least expensive and most commonly used [2,17]. The material is usually applied directly to the patient and molded to the skull defect using free-hand cranioplasty, which often results in a suboptimal cosmetic result (Fig. 1).

Better cosmetic and very good functional results can be achieved using preoperatively designed patient specific implants (PSIs) that have a low complication rate [5,18]. Different materials have been used for this purpose, all with good results. The most commonly used are titanium and polyether-ether-ketone (PEEK) [12]. To achieve optimal cosmetic and functional results at a similar cost as the PMMA implants we developed a technique of intraoperative molding of a PMMA implant on a patient-specific mold [11]. To evaluate the functional and cosmetic outcome of these patients, we performed a retrospective analysis of a consecutive series of 28 patients.

METHODS AND MATERIALS

Patients

Between February 2009 and March 2012 we performed 28 plastic reconstructions of the skull using the patient-specific molded implant (PSMI) technique. Of these patients, 11 were female and 17 male. Indications for cranial reconstruction using artificial material were: resorption of the reimplanted autologous bone flap in 12 patients (42.8%), infection of the autologous bone so it could not be reimplanted in 9 patients (32.1%), infiltration by

tumor in 3 patients (10.7%), loss of the autologous bone following inter-hospital transfer in 3 patients (10.7%), and collapse and instability of the reimplanted bone flap in one patient (3.6%).

Creation of mold template

The mold template was created using high-resolution computed tomography (CT) scans of each patient. Two different techniques were used for making the mold: Subtraction of post-explantation CT from a pre-explantation CT, if available, or subtraction from the mirrored contralateral side. If available scans were of adequate quality (at least 2.5 mm slice thickness), no new scans were acquired to reduce costs and patients' radiation dose. In most of the cases an emergency CT scan of adequate quality (1.27 mm slice thickness), which was acquired before hemicraniectomy, was available and served as pre-explantation CT.

There were two variants for creation of the mold, referred to as Variant A and Variant B.

Variant A:

The CT scans were loaded into the BrainLab iPlan neuronavigation software (Version 3.0, BrainLab, Feldkirchen, Germany). After image fusion of the available scans a 3D-volume rendering was performed using Hounsfield thresholding ($200 > I(x,y,z) > 3071$). Partially resorbed bone, drainages and other objects were manually erased from the object until a perfect 3D model of the skull and the bony defect was created.

Using the same procedure a second 3D model of the intact skull was created using the pre-explantation CT. Then the second model was digitally subtracted from the first, resulting in a 3D model of the intended PSMI. The model of the intact skull was digitally filled out and the model of the PSMI was subtracted. This resulted in a digital version of the mold for creation of the Palacos-PSMI (Fig. 2). To reduce material needed for 3D printing, non-required parts such as the contralateral side were removed, leading to a mold that showed about one centimeter of the surface of the surrounding bone.

Variant B:

If no pre-explantation CT was available, the 3D model of the skull with the bony defect was mirrored and manually adjusted to meet the shape of the opposite side using iPlan. Then the resulting mirrored object was shrunk by 3-4 mm (the intended thickness of the resulting PSMI) and fused to the non-mirrored 3D model, resulting in a mold for PSMI creation. The mold was then isolated from the intact parts of the skull, which are irrelevant for the creation of the PSMI, using the split-tool of iPlan.

The resulting object was exported as a STL-file ("Surface Tesselation Language" 3D file format) and transferred to a 3D-printer (Spectrum Z^{TM} 510 printer by ZCorporation), a high-speed printing device allowing the production of pieces up to 300x200x300 mm with a resulting printing resolution of 0.1 mm. It uses standard inkjet printing technology to create parts layer-by-layer by depositing a liquid binder onto thin layers of powder. After completion of the printing process and drying of the binder solution, excessive powder material around the template model was removed and the mold was infiltrated with polyurethane.

Intraoperative workflow

The mold was brought into the sterile area of the OR in an airtight sterile plastic bag, in which plastic tubing was previously inserted and connected to a vacuum suction device (Fig. 3A). After activation of the suction the plastic bag neatly covered the surface of the mold (Fig 3B). The PSMI was then formed from polymethylmethacrylate bone cement (PMMA) on the sterile surface of the mold (Fig. 3C). After hardening of the PSMI a series of holes was drilled into it to allow exchange of fluid or blood between the epidural and the subgaleal space and to facilitate fixation of the dura at the implant through tissue growth into the holes (Fig. 3D). The PSMI was then fixed into the bony defect using titanium plates and screws (Fig. 3E).

Postoperative neuroimaging

Postoperative CT was performed in case of clinical necessity (e.g. headache onset) to rule out complications such as epidural hematomas or hygromas requiring revision. In cases

with perfect clinical and cosmetic results, we dispensed with postoperative imaging to reduce unnecessary application of radiation to the patients.

Patients' subjective assessments of implant quality

To judge the cosmetic results of the PSMI implantations all patients were asked to answer a catalogue of questions concerning their subjective estimation of their status at least 3 months postoperatively. 17 patients (61%) filled in the questionnaire. One patient could not be contacted postoperatively as he moved to an unknown address. The questions were the following: General satisfaction with the result of the surgery, satisfaction with the cosmetic result, peculiarity of scars, satisfaction with skull shape, symmetry, and palpable gaps or tiers around the implant (each indicated with an ordinal 6-step scale from very poor to excellent). Finally, the patients were asked to judge their general condition pre- and postoperatively (6-step scales from very poor to excellent). Statistical significance was tested using two-sample Wilcoxon test. P-values below 0.05 were considered significant.

Objective assessments of implant quality – Volumetric bone flap subtraction

The available postoperative CT scans for 19 patients (68%) were closely examined and parameters were measured to judge the objective quality and fit of the implant. A volumetric reconstruction of the implanted PSMI and surrounding skull (Hounsfield units 200 to 3071) was subtracted from the 3D model of the ideal flap (result of step 1 in Fig. 2). In case of a perfectly sized, shaped and implanted PSMI this should lead to a complete extinction of the ideal flap model, with a volume of 0 cm^3. The other extreme, in which there was no overlap of the two structures, would be the full volume of the flap model. The resulting volume was set in relation to the volume of the ideal flap model to achieve a result independent from the size of the implanted PSMI (Fig. 4). The result is subtracted from 1 and multiplied by 100 to generate a "quality grade" ranging from 0 (no overlapping between PSMI and ideal flap model) to 100 (perfect size, shape and implantation).

Gaps between bone and PSMI implant were measured in axial planes at three spots: Postero-superior (parietal), antero-superior (frontal) and antero-inferior (fronto-orbital),

in millimeters. There were no measurements in the temporal region, as the implants were mostly not designed to cover the inferior portion of the temporal decompression. In addition to gaps, the thickness of tiers was measured in millimeters. The thickness of the PSMI was measured in millimeters via axial CT in the center of the implant and on the corresponding contralateral side.

Objective assessments of implant quality – Calculation of the dice similarity coefficient

A standardized procedure to measure identity of two volumetric objects is calculation of the dice similarity coefficient (DSC) [20] according to the following formula:

$DSC = 2 (A \cap B) / (A + B)$

DSC: Dice similarity coefficient

A: Volume (cm^2) of the ideal flap model

B: Volume (cm^2) of the implanted PSMI

Values range between 0 (no overlapping of two objects) and 1 (perfect match).

RESULTS

Surgical outcome and complications

All patients recovered well from surgery. One case of postoperative epidural hematoma required surgical revision. One patient with delayed epidural hematoma was readmitted from rehabilitation because of new hemiparesis and deterioration of vigilance; she was successfully treated by trepanation and evacuation of a chronic hematoma at the center of the PSMI and implantation of an epidural drain for 48 hours. In one patient a subcutaneous cerebrospinal fluid (CSF) collection was alleviated after transdermal puncture and evacuation. In another patient the CSF collection slowly regressed without treatment. In one further patient conservative treatment of a subcutaneous CSF collection was not successful and the patient recovered well after implantation of a VP shunt on the contralateral side. Two patients experienced wound-healing disturbances with opening of

the scar over the titanium plates. Both showed no signs of local or systemic infection. In both patients the PSMI was removed and a new one was created using the same mold four weeks later. One of them recovered well, but the other suffered repeated wound healing disturbances and required repeated revision of the implant and closure of the skin using free tissue transplants (Table 1).

Cosmetic results

In general, the patients judged the surgical results as good (Fig. 5). Both patients with wound healing disturbances found their result 'good'. Two of the patients with postoperative subcutaneous CSF collections found their result even 'excellent'. Most patients found their cosmetic result acceptable and scars, skull shape and symmetry of the head 'good'. Figure 6 shows 3D reconstructions of case 25, who judged skull shape, symmetry and gaps and tiers to be 'very poor'. However, to the observer the result does not look bad.

Other clinical results

There was a significant improvement in the general condition in our cohort of PSMI patients ($p=0.024$, Fig. 7). The one patient who reported that his general condition deteriorated postoperatively, from excellent to very poor, is the same patient who judged his cosmetic results as poor (Fig. 6).

Objective assessment of PSMI quality in postoperative CT scan – Volumetric bone flap subtraction

The median volume of the ideal flap was 98.3 cm^3 (SD 34.9). After subtraction of the volumetric reconstruction of the implanted PSMI and surrounding bone the median overlapping volume was 22.3 cm^3 (SD 18.5). The median calculated objective quality grade was 80 (SD 18.0, Table 2).

Gaps and tiers were smallest in the postero-superior (parietal) region, where an average gap of 2.2 mm (SD 2.1) and a median of 1.5 mm were measured. Tiers were mainly inward (average 0.9 mm, SD 0.9, median 1.2 mm). In the antero-superior (frontal)

location the average gap was 3.5 mm (SD 5.7, median 1.7 mm) and the tier was 0.2 mm outward (SD 1.1, median 0 mm). In the antero-inferior (fronto-orbital) location the average gap was 3.8 mm (SD 2.7, median 3.5 mm) and the average inward tier 0.1 mm (SD 1.0, median 0.0 mm, Table 2).

The thickness of the PSMIs corresponded well with the thickness of the contralateral bone. The average PSMI thickness was 4.0 mm (SD 0.8, median 3.8 mm, range 3.2 to 6 mm). On the contralateral side the average bone thickness was 4.2 mm (SD 0.9, median 4.0 mm, range 2.7 to 6.1 mm). The average difference between PSMI and contralateral bone thickness was -0.2 mm (SD 0.9, median 0.0 mm, range -2.9 to 1.3 mm, Table 2).

DISCUSSION

Improvements in intensive care as well as neuroimaging and microsurgical techniques have led to a growing number of indications for hard tissue replacement (HTR) in cranial neurosurgery. There are numerous materials available for this purpose, all of which have their individual advantages. The most commonly used and cheapest is polymethylmethacrylate (PMMA) bone cement. It can be formed intraoperatively to fill the bone defect, and is biocompatible and very stable. A disadvantage is that the manually formed bone replacements often have a suboptimal shape, leading to an inferior cosmetic result. An alternative is the use of autologous bone (split grafts) [1], but this is only available for small defects. Other artificial bone replacements can be made of hydroxylapatite (HA) bone cement, which is usually formed on a matrix of titanium mesh (onlay-technique). HA has the benefit that bone can grow into the margins of the bone replacement and improve the stability of the implant over time. Disadvantages are the high costs and the high infection rate in published studies [3,4,6,7,10,14,15]. Patient-specific implants (PSIs) are usually designed based on CT scans of the patients and are provided by specialized companies. They can be made from titanium, polyether-ether-ketone (PEEK), other polymers, PMMA, HA or biocompatible glass ceramic. What they all have in common is that they usually fit into the defect perfectly and lead to an optimal cosmetic result. Unfortunately, the costs for all of them are relatively high and range from 3500 to more than 5000 US$ per piece, depending on the dimensions of the implant and

the material [2,3,8]. Titanium, PEEK and ceramics can be resterilized in case of surgical revision. Titanium has the disadvantage that it conducts cold temperature far better than bone, which can be uncomfortable for patients (Table 3) [2].

Alternatives to commercial PSIs

The only artificial alternatives to commercially available PSIs are hand-made bone replacements from PMMA or HA bone cement. PMMA is particularly inexpensive (less than 500 US$ per piece) and is therefore frequently used even for replacement of large bone defects. To achieve better cosmetic results using this material, several different attempts were made. One very simple approach was to form the bone replacement directly on the explanted bone flap [9]. This technique has the potential disadvantage that a possibly infected bone flap must be brought into the OR and even into direct contact with the PMMA, leading to a risk of infection. Though increased infection was not shown in the small number of published cases using this technique, it remains a possible serious threat for patients. Another idea is to combine the advantages of computer-assisted design with the benefits of intraoperatively formed PMMA implants. Two publications in the literature describe the use of computer-designed molds [5,15]. We independently developed a comparable technique and this report describes the largest consecutive series operated upon using this method. Furthermore, we provide patients' assessments of the cosmetic results and evaluation of postoperative CT scans for a majority of the patients.

Results of patient-specific molded implants

Complications were comparable with those reported for other techniques, including both commercial PSIs and non-commercial implants. Infections related to wound healing over the titanium plates and the screws were easily treated. No complications were directly attributed to the material used or to the technique. Patients were mainly satisfied with the cosmetic results. Few patients complained about asymmetry of their skull and palpable gaps and tiers around the implant. Atrophy of the temporal muscle and poor overall neurological condition or depression might have contributed to this result, but it remains possible that commercial PSIs lead to slightly better cosmetic results. A standard for assessment of the postoperative result does not currently exist, which makes it impossible

to compare the outcomes of the different techniques that have been described in the literature. We performed volumetric subtractions of the postoperative CT scans from the ideal bone flap models, resulting in an objective quality scale ranging from 0 to 100. While the median quality measured by this method was 80, four patients had values of more than 90, indicating nearly absolute identity of the implanted PSMI with what would be an "ideal" implant. Eight patients had values below 70, usually indicating a too thin or too flat PSMI. Of these, 5 patients completed the questionnaire. Only one of them (case 25) judged his cosmetic result as unfavorable. The others found it good or in one case (case 2) even excellent. Only two of the patients (cases 11 and 25) showed clear dissatisfaction with the PSMI implant. In one of them (case 25) the postoperative CT scan corresponded with a relatively low objective rating. In the other case (case 11) we unfortunately did not have a postoperative CT scan available for evaluation. Calculations of the dice similarity coefficient (DSC) corresponded well with the quality scale. Cases with values above 0.7 showed optimal shape and fit of the implant.

A prospective study comparing the results of commercially available PSIs with the PSMI technique reported here and described previously by Lee et al. [15] and Fathi et al. [9] is needed to identify advantages and disadvantages of the techniques.

Conclusions

Implantation of intraoperatively fabricated patient-specific molded implants is a cost-effective and safe technique that leads to good clinical results with a low complication rate. Calculation of the dice similarity coefficient (DSC) and the volumetric subtraction technique presented here were appropriate for judging implant shape and fit.

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Figure Titles and Legends

Fig 1 title: Postoperative CT scan of a free-hand PMMA cranioplasty.

Fig. 1 legend: a) ideal shape of the cranioplasty; b) the achieved shape of the cranioplasty is too flat.

Fig. 2 title: Creation of mold template

Fig. 2 legend: First step: The post-explantation CT is subtracted from the pre-explantation CT. The result is a 3D model of the required PSMI (flap).

Second step: The 3D model of the flap is subtracted from the pre-explantation CT, which is then digitally "filled out". After elimination of non-required parts such as the contralateral side and zygoma the result is a 3D model of the mold.

Fig. 3 title: Intraoperative creation of patient-specific molded implant (PSMI)

Fig. 3 legend: A) The mold was brought into the OR in an air-tight sterile plastic bag (a), which was connected with the vacuum suction using a flexible tube (b).

B) After removal of the air inside the plastic bag using the vacuum suction the plastic neatly covered the mold surface.

C) The PSMI was created from PMMA on the mold's surface.

D) After hardening of the PMMA, holes were drilled into the PSMI.

E) The implant was placed into the defect and was fixed using low-profile titanium plates and screws.

Fig. 4 title: Volumetric bone flap subtraction examples

Fig. 4 legend: A) The 3D reconstruction of the bone after implantation of a PSMI (in white) is subtracted from the 3D model of the ideal bone flap. The resulting volume (yellow) is representative for the "quality" of the PSMI shape. In this example the PSMI is a little too flat in the frontal region, which results in a considerable volume after subtraction (a).

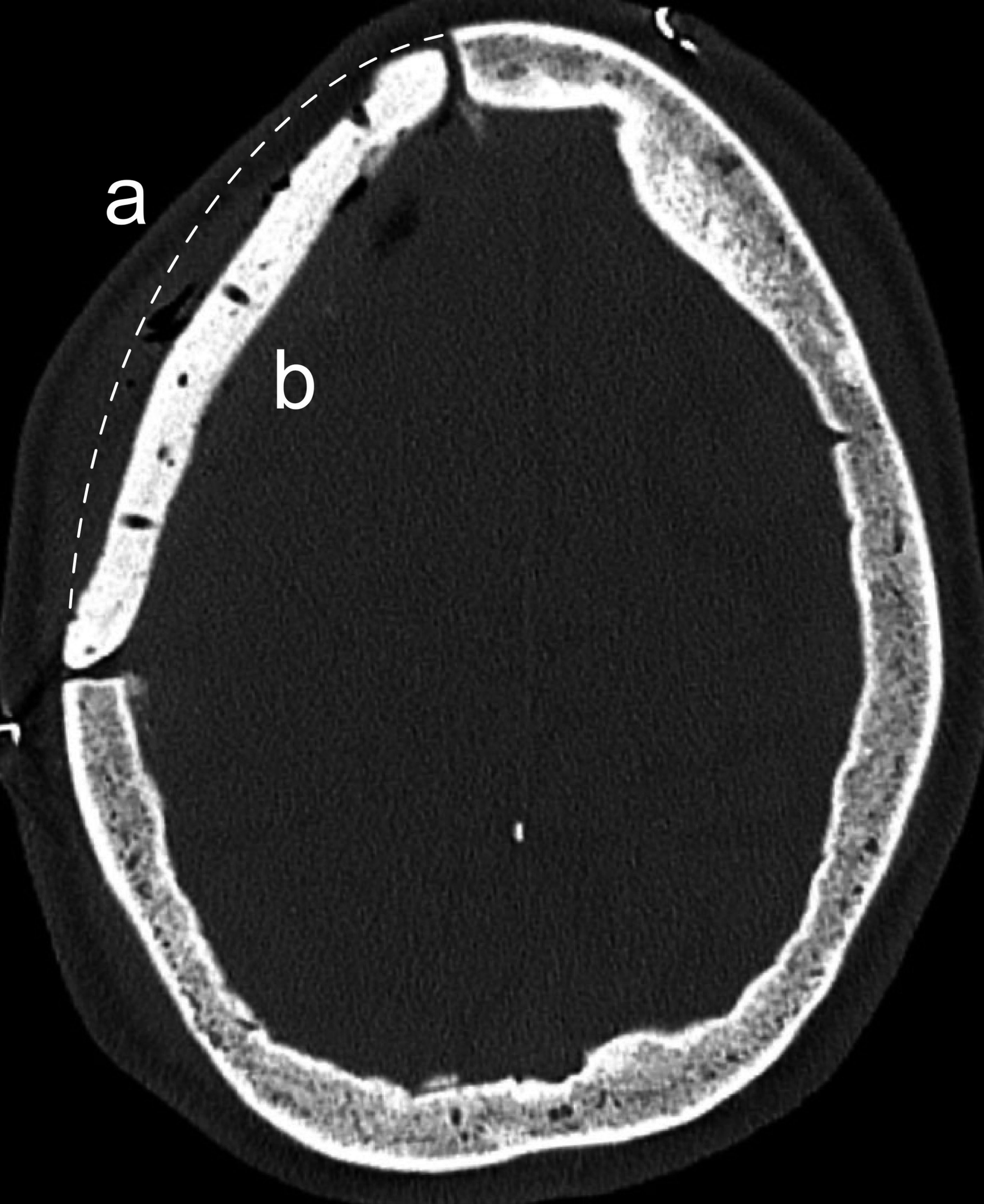
B) In this example the PSMI is not in the perfect position, resulting in a small subtraction volume on the inside (b).

C) In the third example the PSMI is quite well shaped, but very thin compared with the contralateral side. This results in an interior (c) and exterior (d) volume after subtraction. The dura shows signs of calcification (e).
D) In the last example the shape and position of the PSMI are perfect. The outer surface of the implant is optimal. The thickness does not correspond with the contralateral side everywhere, but is absolutely sufficient.

Fig. 5 title: Cosmetic outcome after PSMI implantation
Fig. 5 legend: Patients were asked postoperatively to judge the cosmetic results on ordinal 6-step scales from very poor to excellent. The numbers represent the cases in Table 2.

Fig. 6 title: Illustrative 3D views of case 25
Fig. 6 legend: The 3D reconstructions show the fit of the PSMI of case 25 (see Table 2), who judged gaps and tiers "very poor".
A) Lateral view; B) Frontal view; C) Posterior view; a) titanium low-profile microfixation plates; b) small gap cranial of the petrous bone; c) gap from dehiscent lamdoid suture resulting from the initial trauma; d) reconstruction artifact (scan did not cover the most posterior parts of the skull)

Fig. 7 title: Patients' general conditions before and after PSMI implantation
Fig. 7 legend: Patients were asked pre- and postoperatively to judge their condition on ordinal 6-step scales from very poor to excellent. The numbers represent the cases in Table 2. Only one patient (11) encountered a relevant subjective deterioration.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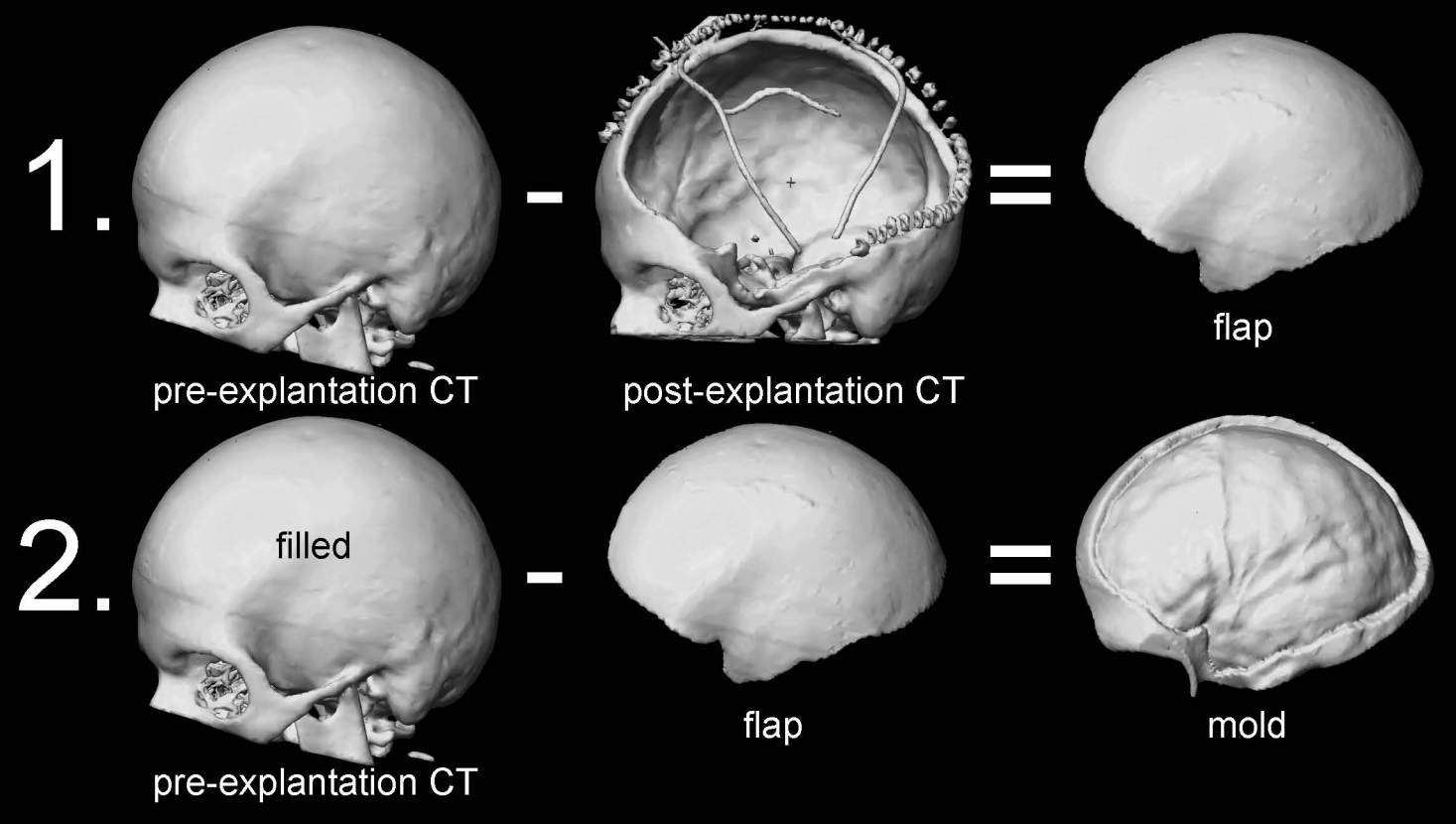
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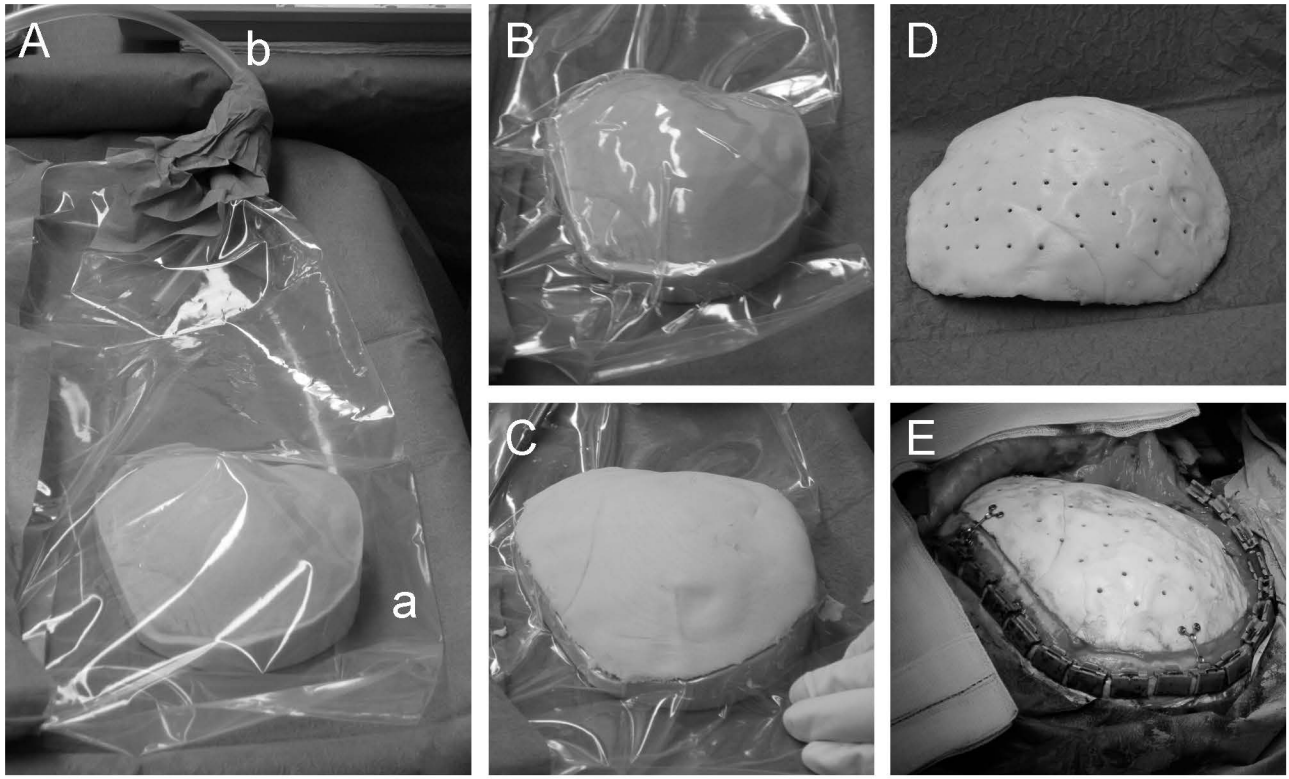
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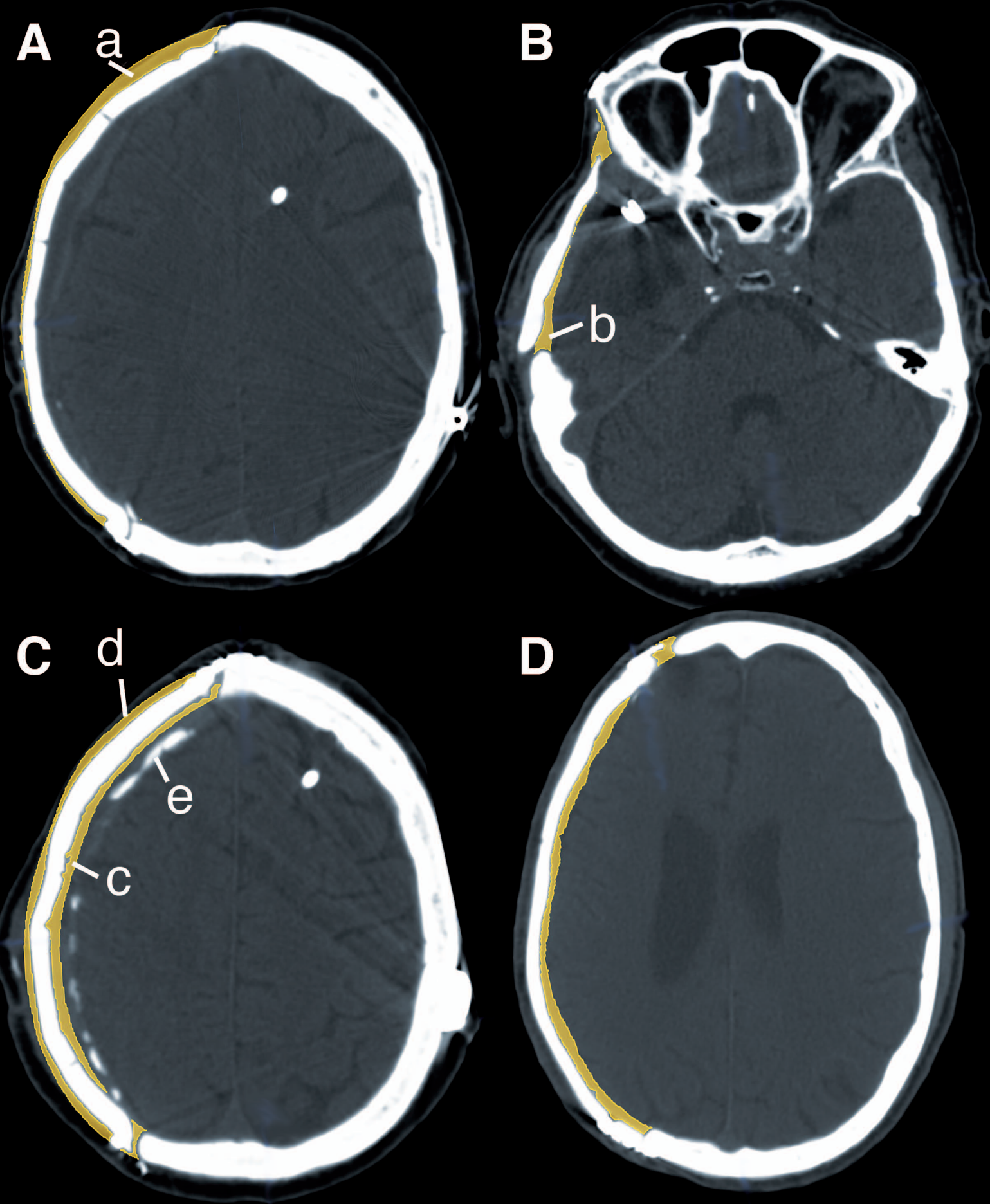
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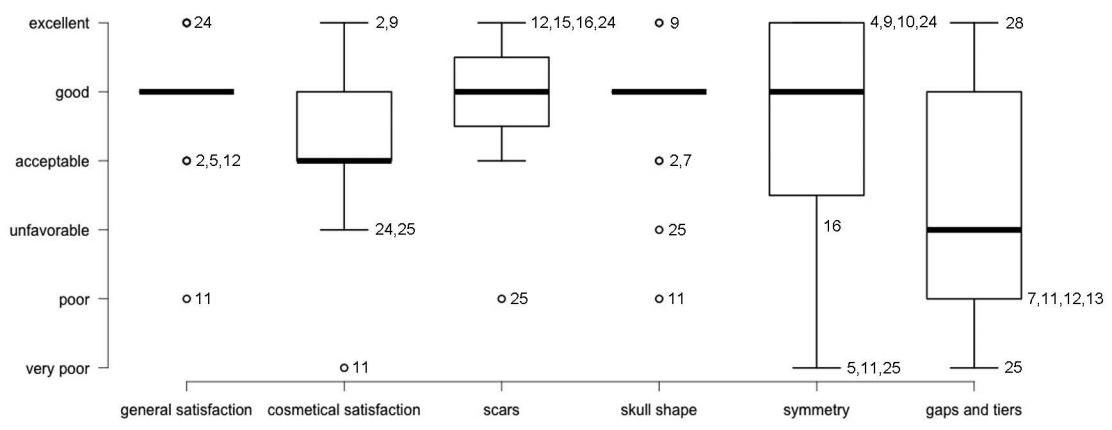
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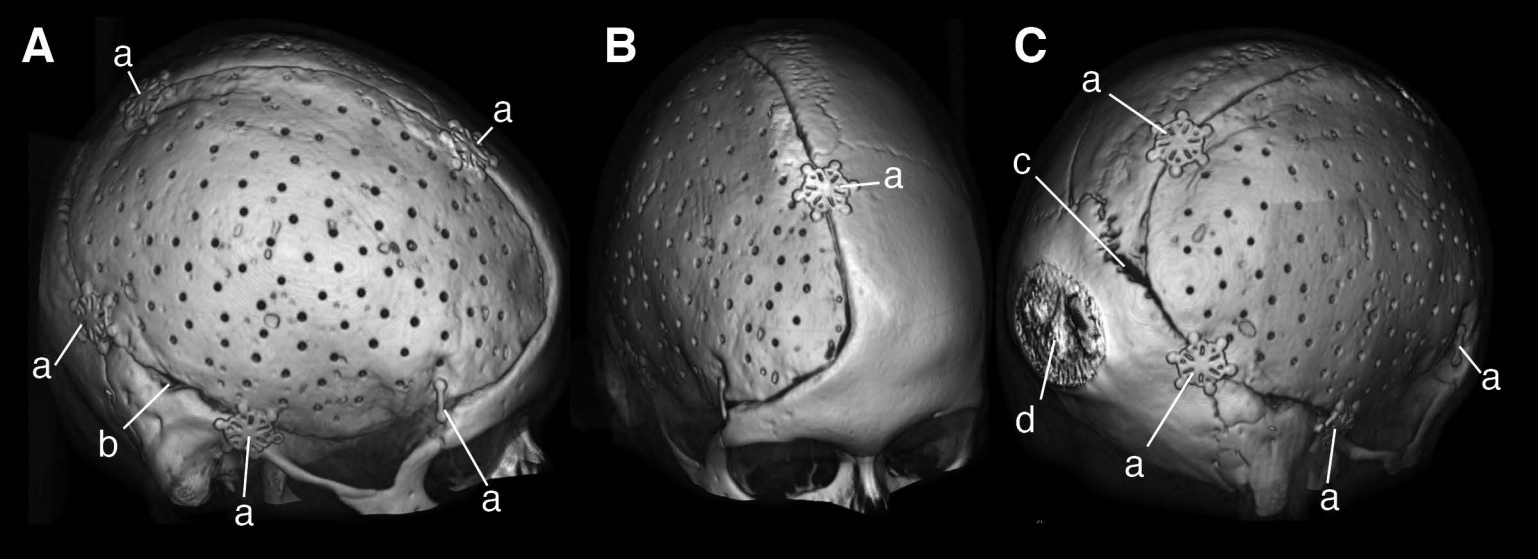
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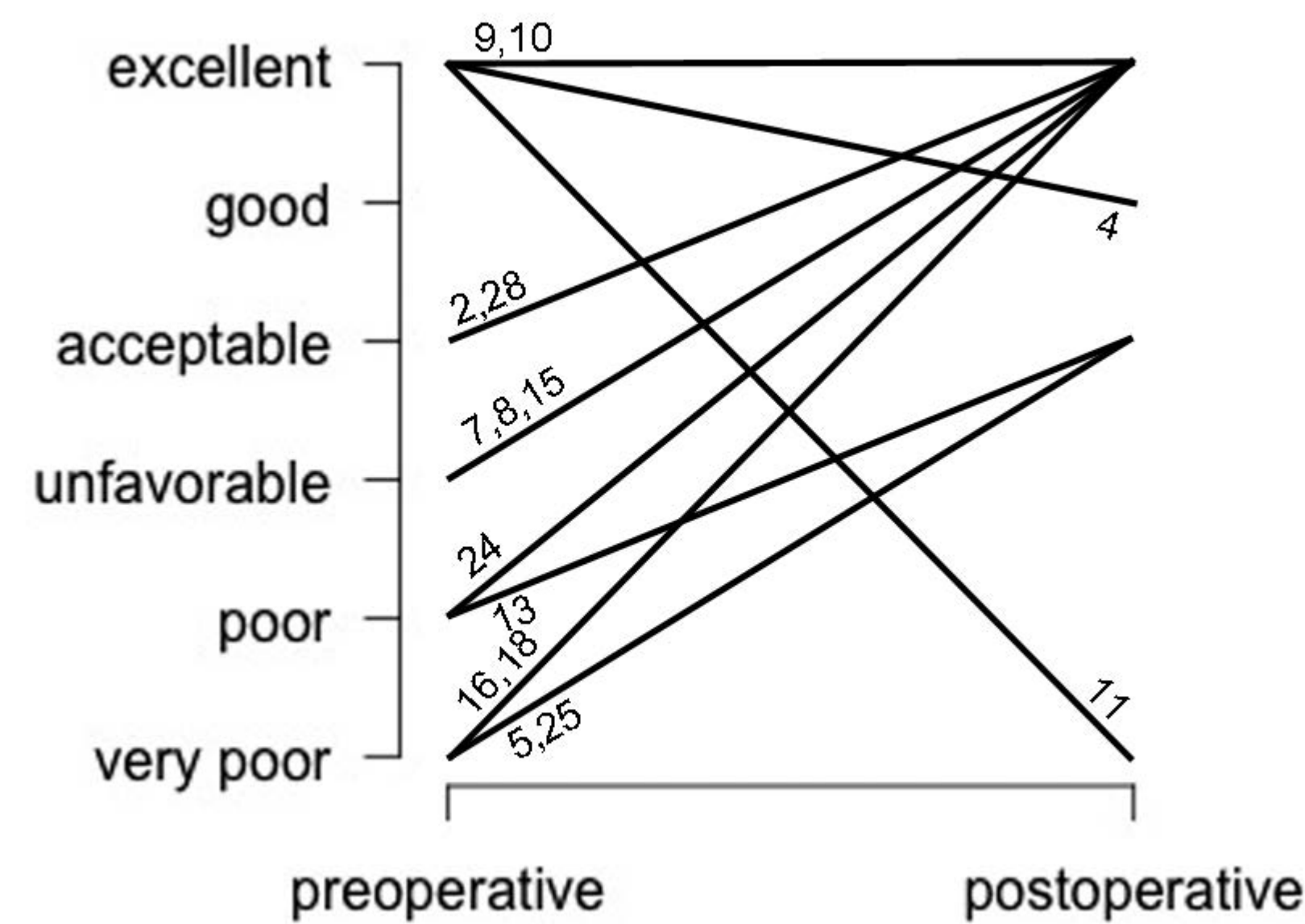
excellent
good
acceptable
unfavorable
poor
very poor
9,10
4
2,28
7,8,15
24
13
16,18
5,25
11
preoperative
postoperative

Table 1: Complications after PSMI implantation

	n	Patient IDs
Infection of unknown origin	0	
Infection after wound healing disturbance	2 (7.1%)	4, 25
Hematoma	2 (7.1%)	5, 23
Hygroma	2 (7.1%)	13, 16
Subcutaneous CSF leak (transient)	1 (3.6%)	24
Subcutaneous CSF leak (persistent)	2 (7.4%)	1, 15
Hydrocephalus	1 (3.7%)	13

Table 1 caption: Incidence of complications after implantation of a PSMI. The patient IDs correspond to the cases in Table 2.

Table 2: Objective judgement of PSMI quality

	Volumetric assessment				Thickness at center		
Nr.	Missing bone volume („ideal flap“) (cm^3)	Overlap (cm^3)	Quality grade (0-100)	DSC (0-1)	PSMI (mm)	Contra-lateral bone (mm)	Relation (%)
1	80.6	6.7	92	0.72	3.5	3.5	100
2	53.3	18.9	65	0.66	3.2	3.2	100
3	88.7	41.9	53	0.6	3.5	3.7	95
4	No postop CT available						
5	67.9	18.2	73	0.69	6.0	4.7	128
6	No postop CT available						
7	93.4	12.1	87	0.69	3.3	2.7	122
8	137.5	24.5	82	0.84	3.2	6.1	52
9-11	No postop CT available						
12	99.7	49.9	50	0.54	3.7	3.7	100
13	125.1	24.8	80	0.71	3.9	4.1	95
14	No postop CT available						
15	128.3	75.6	41	0.38	4.4	4.3	102
16	98.8	7.9	92	0.8	3.6	4.4	82
17	98.3	5.72	94	0.76	5.8	4.0	145
18	No postop CT available						
19	130.0	18.1	86	0.63	3.5	3.9	90
20	46.3	1.1	98	0.77	4.3	4.8	90
21	No postop CT available						
22	91.9	28.1	69	0.66	3.9	3.9	100
23	124.0	21.9	82	0.7	4.0	5.2	77
24	177.7	35.1	80	0.76	4.5	4.6	98
25	135.7	46.1	66	0.68	4.8	5.1	94
26	No postop CT available						
27	88.7	42.6	52	0.52	5.1	3.5	146
28	40.9	22.3	45	0.47	4.1	4.2	98
Mean	100.3	26.4	73	0.66	4.1	4.2	101
Median	98.3	22.3	**80**	**0.69**	3.9	4.1	**98**
SD	34.9	18.5	18	0.12	0.8	0.8	22

Table 2 caption: The result was evaluated by volumetric subtraction of the PSMI from a 3D object representing the missing bone. The overlapping volume was then put in relation with the volume of the missing bone. The resulting quality

grade ranges from 0 to 100. The median result of our cases was 80. The median dice similarity coefficient (DSC) was 0.69. The thickness of the implanted PSMI was measured and put in relation with the contralateral bone. The median thickness was 98%.